K123191

510(k) Summary

As required by 21 CFR Section 807.92(c).

DEC 2 1 2012

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 94089 Phone number: (408) 400-8230 Fax number: (408) 541-6439
Contact:	Kerry J. Flom, Ph.D.
Date of Preparation:	October 9, 2012
Device:	
Trade name:	Xpert® Flu
Common name:	Xpert Flu Assay
Type of Test:	Automated, multiplex real-time reverse transcription-polymerase chain reaction (rRT-PCR) assay intended for the *in vitro* qualitative detection and differentiation of influenza A, influenza B and 2009 H1N1 influenza viral RNA.
Regulation number/ Classification name:	866.3332/Reagents for detection of specific novel influenza A viruses, and 866.3980/Respiratory viral panel multiplex nucleic acid assay
Product code:	OQW, OCC, OOI
Classification Advisory Panel	Microbiology (83)
Predicate Device:	Cepheid Xpert Flu Assay [510(k) #K120911]

Device Description:

The Xpert Flu Assay is a rapid, automated *in vitro* diagnostic test for qualitative detection and differentiation of influenza A, influenza B and influenza A, subtype 2009 H1N1. The assay is performed on the Cepheid GeneXpert Instrument Systems. The GeneXpert Instrument Systems automate and integrate sample purification, nucleic acid amplification, and detection of the target sequence in simple or complex samples using real-time PCR and RT-PCR assays. The systems require the use of single-use disposable cartridges that hold the PCR reagents and host the PCR process. Because the cartridges are self-contained and specimens never come into contact with working parts of the instrument modules, cross-contamination between samples is minimized.

The Xpert Flu Assay includes reagents for the detection and differentiation of influenza A, influenza B and influenza A, subtype 2009 H1N1 directly from nasal aspirates/washes (NA/W) and nasopharyngeal (NP) swab specimens from patients suspected of having influenza. A Sample Processing Control (SPC) and a Probe Check Control (PCC) are also included. The SPC is present to control for adequate processing of the target viruses and to monitor the presence of inhibitors in the PCR reaction. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity and dye stability.

The liquid specimen (NA/W) or swab specimen (NP) is collected according to the institution's standard procedures and placed into Universal Transport Medium (3mL UTM tubes). Following a brief mixing by inverting the UTM tube five times, the eluted material and one single-use reagent (Reagent 1), that is provided with the assay, are transferred to different, uniquely-labeled chambers of the disposable fluidic cartridge (the Xpert Flu cartridge). The user initiates a test from the system user interface and places the cartridge into the GeneXpert instrument platform, which performs hands-off real-time, multiplex polymerase chain reaction (PCR) for detection of DNA. In this platform, additional sample preparation, amplification, and real-time detection are all fully-automated and completely integrated.

The single-use, multi-chambered fluidic cartridges are designed to complete sample preparation and real-time PCR for detection and differentiation of influenza A, influenza B and influenza A, subtype 2009 H1N1 in 75 minutes. The GeneXpert Instrument Systems, which consist of the GeneXpert Dx System, the GeneXpert Infinity-48 System, and the GeneXpert Infinity-80 System, have 1 to 80 randomly accessible modules that are each capable of performing separate sample preparation and real-time PCR tests. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE® thermocycler for performing real-time PCR and detection.

Device Intended Use:

The Cepheid Xpert® Flu Assay, performed on the GeneXpert® Instrument Systems, is an automated, multiplex real-time RT-PCR assay intended for the *in vitro* qualitative detection and differentiation of influenza A, influenza B and 2009 H1N1 influenza viral RNA. The Xpert Flu Assay uses nasal aspirates/washes and nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors. The Xpert Flu Assay is intended as an aid in the diagnosis of influenza.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions.

Performance characteristics for influenza A were established during the 2009-2010 influenza season when 2009 H1N1 influenza was the predominant influenza A virus in circulation. Performance characteristics for influenza A were confirmed when influenza

A/H3 and influenza A/2009 H1N1 were the predominant influenza A viruses in circulation (2009-2010, 2010-2011 and 2011-2012). When other influenza A viruses are emerging, performance characteristics may vary.

If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Substantial Equivalence:

The Xpert Flu Assay is substantially equivalent to the current Xpert Flu Assay [510(k) #K120911].

Similarities and differences between the Cepheid Xpert Flu Assay and the predicate device are shown in Table 5.1.

A clinical comparison study was conducted using prospectively collected archived and/or pre-selected banked specimens to compare the modified Xpert Flu Assay performance to the previously cleared Xpert Flu Assay.

Table 5.1: Comparison of Similarities and Differences of the modified Xpert Flu Assay with the Predicate Device, Xpert Flu Assay

	Device	**Predicate**
Item	**Modified Cepheid Xpert Flu**	**Cepheid Xpert Flu**
510(k) Number	#K123191	#K120911
Regulation	Same	866.3332 and 866.3980
Product Code	Same	OQW, OCC, OOI
Device Class	Same	II
Technology/ Detection	Same	Multiplex real time RT/PCR
Intended Use	The Cepheid Xpert® Flu Assay, performed on the GeneXpert® Instrument Systems, is an automated, multiplex real-time RT-PCR assay intended for the *in vitro* qualitative detection and differentiation of influenza A, influenza B and 2009 H1N1 influenza viral RNA. The Xpert Flu Assay uses nasal aspirates/washes and nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection in	The Cepheid Xpert® Flu Assay is an automated, multiplex real-time RT-PCR assay intended for the *in vitro* qualitative detection and differentiation of influenza A, influenza B and 2009 H1N1 influenza viral RNA. The Xpert Flu Assay uses nasal aspirates/washes and nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors.

	Device	Predicate
Item	**Modified Cepheid Xpert Flu**	**Cepheid Xpert Flu**
	conjunction with clinical and epidemiological risk factors. The Xpert Flu Assay is intended as an aid in the diagnosis of influenza. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2009-2010 influenza season when 2009 H1N1 influenza was the predominant influenza A virus in circulation. Performance characteristics for influenza A were confirmed when influenza A/H3 and influenza A/2009 H1N1 were the predominant influenza A viruses in circulation (2009-2010, 2010-2011 and 2011-2012). When other influenza A viruses are emerging, performance characteristics may vary. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.	The Xpert Flu Assay is intended as an aid in the diagnosis of influenza. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2009-2010 influenza season when 2009 H1N1 influenza was the predominant influenza A virus in circulation. When other influenza A viruses are emerging, performance characteristics may vary. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.
Indication for Use	Same	Patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors.
Assay Targets	Same	Influenza A, influenza B, and influenza A, subtype 2009 H1N1
Specimen Types	Same	Nasal aspirates/washes (NA/W) and Nasopharyngeal (NP) swabs
Technological Principles	Same	RT/PCR
Nucleic Acid Extraction	Same	Yes

	Device	Predicate
Item	**Modified Cepheid Xpert Flu**	**Cepheid Xpert Flu**
Extraction Methods	Same	Sample preparation integrated in GeneXpert Cartridge and GeneXpert Instrumentation System
Assay Results	Same	Qualitative
Instrument System	Same	Cepheid GeneXpert® Instrument Systems
Assay Controls	Same	Encapsulated (armored) RNA pseudovirus as a sample processing control. Available but not provided are inactivated virus controls for Flu A/B and Flu A 2009 H1N1 as external positive controls and Coxsackie virus as an external negative control.
Rapid test results	Same	Total 75 minutes for sample preparation and rRT-PCR
Primers and probes for influenza A, influenza B, and influenza A subtype 2009 H1N1	Same plus an additional primer for Influenza A	Original primers and probes to detect the presence of nucleic acid sequences of influenza A, influenza B, and influenza, subtype 2009 H1N1
Laboratory Users	Same	CLIA Moderate or High Complexity

Non-Clinical Studies:

Analytical Sensitivity

Analytical Reactivity (Inclusivity)

The analytical reactivity of the Xpert Flu Assay was evaluated against forty (40) strains of influenza A (H1N1, H3N2, H5N2, H5N1 and H7N3 subtypes), influenza A 2009 H1N1 and influenza B. Of these, influenza A subtype H1N1 (11), influenza A subtype H3N2 (9), influenza A subtype 2009 H1N1 (6), influenza A subtype H5N1 (1), influenza A subtype H5N2 (1), influenza A subtype H7N3 (1), and influenza B (11) were included. Twelve of the 40 influenza strains evaluated in this study were tested at the LoD concentration while all remaining strains were tested using viral stocks at 5-250 $TCID_{50}$/mL. Three (3) replicates were tested for each strain. Results are shown in Table 5.2.

Table 5.2: Analytical Reactivity (Inclusivity) Results of the Xpert Flu Assay

Viral Strain	Concentration ($TCID_{50}$/mL)	Influenza A	Influenza A 2009 H1N1	Influenza B
Influenza A/Denver/1/57 (H1N1)[a]	250	+	-	-
Influenza A/Hawaii/15/2001 (H1N1)[a]	50	+	-	-
Influenza A/Mal/302/54 (H1N1)[a]	50	+	-	-
Influenza A/New Jersey/8/76 (H1N1)[a]	250	+	-	-
Influenza A/NWS/33 (H1N1)[a]	5	+	-	-
Influenza A/PR/8/34 (H1N1)[a]	50	+	-	-
Influenza A/Taiwan/42/06 (H1N1)[a]	50	+	-	-
Influenza A/Swine/1976/31 (Swine H1N1)[a]	250	+	-	-
Influenza A/Swine/Iowa/15/30 (Swine H1N1)[a]	50	+	-	-
Influenza A/Brisbane/59/07 (H1N1)[a, b]	1	+	-	-
Influenza A/NewCaledonia/20/1999 (H1N1)[a, b]	5	+	-	-
Influenza A/Brisbane/10/07 (H3N2)[b]	1.25	+	-	-
Influenza A/Victoria/361/2011 (H3N2)[b]	1.25	+	-	-
Influenza A/Victoria/3/75 (H3N2)	250	+	-	-
Influenza A/Aichi2/68 (H3N2)	50	+	-	-
Influenza A/Hong Kong/8/68 (H3N2)	50	+	-	-
Influenza A/NewYork/55/2004 (H3N2)	50	+	-	-
Influenza A/Port Chalmers/1/73 (H3N2)	50	+	-	-
Influenza A/Wisconsin/67/05 (H3N2)[b]	10	+	-	-
Influenza A/Perth/16/2009 (H3N2)	50	+	-	-
Influenza A/SwineNY/01/2009 (09 H1N1)[b]	25	+	+	-
Influenza A/SwineNY/02/2009 (09 H1N1)[b]	1.25	+	+	-
Influenza A/SwineNY/03/2009 (09 H1N1)[b]	1.25	+	+	-

Viral Strain	Concentration ($TCID_{50}$/mL)	Influenza A	Influenza A 2009 H1N1	Influenza B
Influenza A/California/7/2009 (09 H1N1)	5	+	+	-
Influenza A/Canada/6294 (09 H1N1)	50	+	+	-
Influenza A/Wisconsin/629-S1 (09 H1N1)	1	+	+	-
Influenza A/Mallard/WI/34/75 (H5N2)	3 pg/µL[c]	+	-	-
Influenza A/Anhui/02/2005/PR8-IBCDC-RG5 (H5N1)	0.122 pg/µL[c]	+	-	-
Influenza A/chicken/NJ/15086-3/94 (H7N3)	50 pg/µL[c]	+	-	-
Influenza B/Allen/45	50	-	-	+
Influenza B/Florida/02/06[b]	5	-	-	+
Influenza B/Florida/04/06	50	-	-	+
Influenza B/Florida/07/04[b]	5	-	-	+
Influenza B/GL/1739/54	50	-	-	+
Influenza B/Hong Kong/5/72	50	-	-	+
Influenza B/Lee/40	50	-	-	+
Influenza B/Malaysia/2506/04	50	-	-	+
Influenza B/Maryland/1/59	5	-	-	+
Influenza B/Panama/45/90	250	-	-	+
Influenza B/Taiwan/2/62	50	-	-	+

[a]Seasonal influenza A H1N1 (not 2009 H1N1)
[b]Strains (12) used in analytical LOD study and tested at limit of detection
[c]Concentration expressed in picograms/µL

Analytical Sensitivity

Limit of Detection

Studies were performed to determine the analytical limit of detection (LoD) of 2 seasonal influenza A (H1N1), 3 seasonal influenza A (H3N2), 5 influenza A 2009 H1N1 and 2 influenza B strains diluted into a surrogate nasopharyngeal matrix. The surrogate matrix consisted of 1% human blood, 2.5% mucin and 0.85% sodium chloride. The LoD is defined as the lowest concentration (tissue culture infective dose $[TCID]_{50}$/mL) per sample that can be reproducibly distinguished from negative samples with 95%

confidence or the lowest concentration at which 19 of 20 replicates were positive. Each strain was tested in replicates of 20 per concentration of virus.

The LoD was determined empirically as the first concentration that had 19/20 or 20/20 positive results. The LoD values for each strain tested are summarized in Tables 5.3 – 5.6.

Table 5.3: Confirmed LoD ($TCID_{50}$/mL) – Seasonal Influenza A H1N1

Strain ID – Influenza A subtype H1N1	Confirmed LoD ($TCID_{50}$/mL) (at least 19/20 positive)
Influenza A/H1/Brisbane/59/07	1 (20/20)
Influenza A/H1/New Caledonia/20/1999	5 (20/20)

Table 5.4: Confirmed LoD ($TCID_{50}$/mL) – Seasonal Influenza A H3N2

Strain ID – Influenza A subtype H3N2	Confirmed LOD ($TCID_{50}$/mL) (at least 19/20 positive)
Influenza A/H3/Brisbane/10/07	1.25 (20/20)
Influenza A/Victoria/361/2011	1.25 (20/20)
Influenza A/H3/Wisconsin/67/05	10 (20/20)

Table 5.5: Confirmed LoD ($TCID_{50}$/mL) – Influenza A 2009 H1N1

Strain ID – Influenza A subtype 2009 H1N1	Confirmed LOD ($TCID_{50}$/mL) (at least 19/20 positive)
Influenza A/SwineNY/01/2009 (Lot #1)	25 (19/20)
Influenza A/SwineNY/01/2009 (Lot #2)	0.125 (19/20)
Influenza A/SwineNY/02/2009	1.25 (20/20)
Influenza A/SwineNY/03/2009	1.25 (20/20)
Influenza A/Canada/6294/2009	35 (19/20)
Influenza A/WI/629-S1/2009 (D00015)	1 (20/20)

Table 5.6: Confirmed LoD ($TCID_{50}$/mL) – Influenza B

Strain ID – Influenza B	Confirmed LOD ($TCID_{50}$/mL) (at least 19/20 positive)
Influenza B/Florida/02/06	2 (19/20)
Influenza B/Florida/07/04	5 (20/20)

Analytical Specificity (Exclusivity)

The analytical specificity of the Xpert Flu Assay was evaluated by testing a panel of 40 cultures consisting of 18 viral, 21 bacterial, and one yeast representing common respiratory pathogens or those potentially encountered in the nasopharynx. Three replicates of all bacterial and yeast strains were tested at concentrations $\geq 10^6$ CFU/mL. Three replicates of all viruses were tested at concentrations $\geq 10^4$ $TCID_{50}$/mL. Purified nucleic acids (copies/mL) were tested for one virus strain (Cytomegalovirus) and one bacterial strain (*Bordetella pertussis*). Positive and negative controls were included in the study. The analytical specificity was 100%. Results are shown in Table 5.7.

Table 5.7: Analytical Specificity for Xpert Flu Assay[a]

Strain	Concentration (per Cartridge)	Influenza A	Influenza A 2009 H1N1	Influenza B
Positive Control 1 – Influenza A/Influenza B	N/A[b]	+	-	+
Positive Control 2 – Influenza A 2009 H1N1	N/A[b]	+	+	-
Negative Control	N/A[b]	-	-	-
Adenovirus Type 7A	1.1×10^5 $TCID_{50}$/mL	-	-	-
Adenovirus Type 1	1.0×10^7 $TCID_{50}$/mL	-	-	-
Human Coronavirus 229E	2.5×10^4 $TCID_{50}$/mL	-	-	-
Human Coronavirus OC43	5.6×10^4 $TCID_{50}$/mL	-	-	-
Cytomegalovirus[c]	4.7×10^7 Copies /mL	-	-	-
Enterovirus Type 71	3.5×10^5 $TCID_{50}$/mL	-	-	-
Epstein-Barr Virus	7.1×10^8 $TCID_{50}$/mL	-	-	-
Parainfluenzavirus Type 1	1.1×10^5 $TCID_{50}$/mL	-	-	-

Strain	Concentration (per Cartridge)	Influenza A	Influenza A 2009 H1N1	Influenza B
Parainfluenzavirus Type 2	3.1×10^7 $TCID_{50}$/mL	-	-	-
Parainfluenzavirus Type 3	1.9×10^6 $TCID_{50}$/mL	-	-	-
Measles Virus	6.3×10^4 $TCID_{50}$/mL	-	-	-
Human Metapneumovirus	3.8×10^5 $TCID_{50}$/mL	-	-	-
Mumps Virus	6.3×10^6 $TCID_{50}$/mL	-	-	-
Respiratory Syncytial Virus A	5.3×10^7 $TCID_{50}$/mL	-	-	-
Respiratory Syncytial Virus B	1.2×10^7 $TCID_{50}$/mL	-	-	-
Human HSV Type 1	3.1×10^6 $TCID_{50}$/mL	-	-	-
Human Rhinovirus Type 4	1.2×10^5 $TCID_{50}$/mL	-	-	-
Echovirus 11	3.3×10^8 $TCID_{50}$/mL	-	-	-
Bordetella pertussis[c]	5000 ng/mL	-	-	-
Chlamydia pneumoniae	5×10^6 CFU/mL	-	-	-
Corynebacterium xerosis	1×10^6 CFU/mL	-	-	-
Escherichia coli	1×10^6 CFU/mL	-	-	-
Proteus vulgaris	1×10^6 CFU/mL	-	-	-
Proteus mirabilis	1×10^6 CFU/mL	-	-	-
Klebsiella pneumoniae	1×10^6 CFU/mL	-	-	-
Haemophilus influenzae	1×10^6 CFU/mL	-	-	-
Lactobacillus crispatus	1×10^6 CFU/mL	-	-	-
Legionella pneumophila	1×10^6 CFU/mL	-	-	-
Moraxella catarrhalis	1×10^6 CFU/mL	-	-	-
Mycobacterium tuberculosis (BCG strain)	1×10^6 CFU/mL	-	-	-
Mycoplasma pneumoniae	1×10^6 CFU/mL	-	-	-
Neisseria meningitides	1×10^6 CFU/mL	-	-	-
Neisseria cinneria	1×10^6 CFU/mL	-	-	-
Pseudomonas aeruginosa	1×10^6 CFU/mL	-	-	-

Strain	Concentration (per Cartridge)	Influenza A	Influenza A 2009 H1N1	Influenza B
Staphylococcus aureus	$1x10^6$ CFU/mL	-	-	-
Staphylococcus epidermidis	$1x10^6$ CFU/mL	-	-	-
Streptococcus pneumoniae	$1x10^6$ CFU/mL	-	-	-
Streptococcus pyogenes	$1x10^6$ CFU/mL	-	-	-
Streptococcus salivarius	$1x10^6$ CFU/mL	-	-	-
Candida albicans	$1x10^6$ CFU/mL	-	-	-

[a]Cross reactivity with other swine-origin strains has not been tested.
[b]Concentration not available because these are inactivated viruses.
[c]Nucleic acid was tested for Cytomegalovirus and *Bordetella pertussis.*

Interfering Substances

Potentially interfering substances that may be present in the nasopharynx were evaluated on representative Flu strains directly relative to the performance of the Xpert Flu Assay. Potentially interfering substances in the nasopharynx may include, but are not limited to: blood, nasal secretions or mucus, and nasal and throat medications used to relieve congestion, nasal dryness, irritation, or asthma and allergy symptoms, as well as antibiotics and antivirals. These substances are listed in Table 5.8 with active ingredients and concentrations tested shown. Highly viscous samples resulting from the addition of 1.5% (w/v) and 2.5% (w/v) mucin yielded false-negative test results from the Xpert Flu Assay. Inhibition of the Xpert Flu Assay was also observed from the addition of 1% (w/v) mucin, resulting in delayed detection of influenza A, influenza A subtype 2009 H1N1, and influenza B.

Table 5.8: Potentially Interfering Substances in Xpert Flu Assay.

Substance	Description/Active Ingredient	Concentration Tested in one or more Flu strains
Blood (human)	N/A	2% (v/v)
Mucin	Purified mucin protein (Bovine or porcine submaxillary gland)	2.5%, 1.5%, 1%, and 0.5% (w/v)
Neo-Synephrine® Nasal Drops	Phenylephrine HCl	15% (v/v)
Anefrin Nasal Spray	Oxymetazoline Hydrochloride	15% (v/v)
Zicam® Nasal Gel	Luffa opperculata, Galphimia glauca, Histaminum hydrochloricum Sulfur	5% (v/v)
Saline Nasal Spray	Sodium Chloride with preservatives	15% (v/v)
Antibiotic, nasal ointment	Mupirocin	10 mg/mL
Antibacterial, systemic	Tobramycin	4.0 µg/mL
Antiviral	Oseltamivir (TamiFlu)	7.5 mg/mL

Substance	Description/Active Ingredient	Concentration Tested in one or more Flu strains
Throat lozenges, oral anesthetic and analgesic	Menthol	1.7 mg/mL menthol

Carry-Over Contamination Study

Please refer to the previously FDA-cleared 510(k) #K103766 for additional information.

Linearity

Please refer to the previously FDA-cleared 510(k) #K103766 for additional information.

Clinical Performance Characteristics:

Reproducibility

Please refer to the previously FDA-cleared 510(k) #K103766 for additional information.

Instrument System Reproducibility

Please refer to the previously FDA-cleared 510(k) #K103766 and #K120911 for additional information.

Clinical Performance Characteristics

Clinical Performance Study

Performance characteristics for influenza A were established during the 2009-2010 influenza season when 2009 H1N1 influenza was the predominant influenza A virus in circulation. Performance characteristics for influenza A were confirmed when influenza A/H3 and influenza A/2009 H1N1 were the predominant influenza A viruses in circulation (2009-2010, 2010-2011 and 2011-2012).

Specimens included frozen leftover, prospectively collected, unlinked prospectively collected archived and/or pre-selected banked nasal aspirates/washes (NA/W) and nasopharyngeal (NP) swab specimens collected as standard of care (SOC) for patients suspected of influenza infection.

Additionally, ten contrived specimens (five each, NP swab and NA/W) were prepared and tested during this study. Specimens consisted of influenza A/Victoria/361/2011 (H3H2) strain spiked into NP and NA/W matrices, and were included due to the potential low prevalence of this strain in the archived specimen set. These ten specimens (tested

blindly as part of the overall specimen cohorts) are analyzed separately and not included in the primary dataset.

The modified Xpert Flu Assay performance was compared to the current Xpert Flu Assay. Sequencing was performed for all discrepant specimens.

Overall Results

Relative to the Xpert Flu Assay, the modified Xpert Flu Assay demonstrated a positive and negative agreement for detection of influenza A with NA/W specimens of 100% and 98.1%, respectively (Table 5.9). The modified Xpert Flu Assay positive and negative agreement for influenza A subtype 2009 H1N1 with NA/W specimens were 97.1% and 99.6% (Table 5.9). The modified Xpert Flu Assay positive and negative agreement for influenza B with NA/W specimens were 100% and 99.6%, respectively (Table 5.9).

Relative to the Xpert Flu Assay, the modified Xpert Flu Assay demonstrated a positive and negative agreement for detection of influenza A with NP swabs of 100% and 95.2%, respectively (Table 5.9). The modified Xpert Flu Assay positive and negative agreement for influenza A subtype 2009 H1N1 with NP swabs were 98.5% and 99.6% (Table 5.9). The modified Xpert Flu Assay positive and negative agreement for influenza B with NP swabs were 100% and 99.1%, respectively (Table 5.9).

Table 5.9: Xpert Flu Assay Performance on Prospectively Collected Archived NA/W and NP Swab Specimens

Specimen Type	Target	n	TP	FP	TN	FN	Positive Agreement % (95 CI)	Negative Agreement % (95 CI)
NA/W	Flu A	302	145	3[a]	154	0	100 (97.5-100)	98.1 (94.5-99.6)
	H1N1	302	66	1[b]	233	2[b]	97.1 (89.8-99.6)	99.6 (97.6-100)
	Flu B	302	22	1[c]	279	0	100 (84.6-100)	99.6 (98.0.-100)
NP Swab	Flu A	352	165	9d	178	0	100 (97.8-100)	95.2 (91.1-97.8)
	H1N1	352	67	1[b]	283	1[b]	98.5 (92.1-100)	99.6 (98.1-100)
	Flu B	352	27	3[b]	322	0	100 (87.2-100)	99.1 (97.3-99.8)

[a]Discrepant testing results by sequencing: 2 of 3 Flu A/Perth/16/2009-like; 1 of 3 no sequencing results available.
[b]Discrepant testing results by sequencing: no sequencing results available.
[c]Discrepant testing results by sequencing: Flu B.
[d]Discrepant testing results by sequencing: 4 of 9 Flu A/Victoria/361-like; 1 of 9 Flu A/Perth/16/2009-like; 4 of 9 no sequencing results available.

Contrived Specimens

As expected the ten contrived specimens were Flu A Positive; 2009 H1N1 NOT DETECTED; Flu B Negative by the modified Xpert Flu Assay, and Flu A Negative;

2009 H1N1 NOT DETECTED; Flu B Negative by the current Xpert Flu Assay. Sequencing results for all ten of these specimens were positive for the A/Victoria/361/2001 strain of influenza.

Conclusions

The results of the nonclinical analytical and clinical performance studies summarized above demonstrate that the modified Xpert Flu Assay is substantially equivalent to the predicate Xpert Flu Assay.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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Document Control Center – WO66-G609
Silver Spring, MD 20993-002

Cepheid
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DEC 2 1 2012

Re: K123191
Trade/Device Name: Xpert® Flu
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OCC, OQW, OOI
Dated: October 9, 2012
Received: October 11, 2012

Dear Dr. Flom:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Uwe Scherf for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

4.0 Indications for Use

Indications for Use Form

510(k) Number (if known): K123191

Device Name: Xpert® Flu

Indications for Use:

The Cepheid Xpert® Flu Assay, performed on the GeneXpert® Instrument Systems, is an automated, multiplex real-time RT-PCR assay intended for the *in vitro* qualitative detection and differentiation of influenza A, influenza B and 2009 H1N1 influenza viral RNA. The Xpert Flu Assay uses nasal aspirates/washes and nasopharyngeal swab specimens collected from patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors. The Xpert Flu Assay is intended as an aid in the diagnosis of influenza.

Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions.

Performance characteristics for influenza A were established during the 2009-2010 influenza season when 2009 H1N1 influenza was the predominant influenza A virus in circulation. Performance characteristics for influenza A were confirmed when influenza A/H3 and influenza A/2009 H1N1 were the predominant influenza A viruses in circulation (2009-2010, 2010-2011 and 2011-2012). When other influenza A viruses are emerging, performance characteristics may vary.

If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Prescription Use ___X____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

Tamara Fields -S

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K123191